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10/589,533	05/15/2007	David Wynick	68150.000003	8463

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EXAMINER	
MACFARLANE, STACEY NEE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,533	WYNICK, DAVID	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-48,54-63 and 96-100* is/are pending in the application.

4a) Of the above claim(s) *33-48,54-63 and 96-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, identified as Claims 17-32, and the species multiple sclerosis, in the reply filed on June 5, 2009 is acknowledged. The traversal is on the ground(s) that the "special technical feature of claim 1 [Examiner assumes Applicant means claim 17 since claim 1 is cancelled] is the use of GALR2-specific agonist compounds and their use in the treatment of brain injury, damage or disease ... Liu is silent on the technical feature of claim 1. In particular, Liu discuses the use of a GALR2-agonist in the spinal cord for the treatment of neuropathic pain does not discuss treating brain injury, damage, or disease comprising administering a GALR2-specific agonist. Rather, Liu discloses the analgesic effects of AR-M1896 and AR-M961 and is silent on the claimed uses of treating brain injury, damage, or disease comprising administering a GALR2-specific agonist". This is not found persuasive because neuropathic pain accompanying spinal cord injury is a central processing or "brain" disorder arising from damage to the nerve fibers, which send incorrect signals to the pain centers of the brain. Depending claims define the brain injury or damage as being caused by "direct or indirect trauma or surgery to the brain or spinal cord" (claim 18). Therefore, in the broadest reasonable interpretation of the claims, Liu teaches the special technical feature of the first claim, claim 17. The species election is traversed because: "The Restriction Requirement did not elucidate reasons and examples as required by MPEP § 808.02 to support a species election between the brain injury, brain damage, and brain disease as listed in claims 18-22. MPEP § 806.04(b). A requirement

for restriction is permissible if there is a patentable difference between the species as claimed and there would be a serious burden on the Examiner if restriction was not required. MPEP § 808.01(a) [R-5]". Applicant further traverses that the neurodegenerative diseases listed in claim 22 are in the same classification and therefore do not occupy a separate status in the art. While this has been carefully considered it is not found persuasive because Examiner has provided reasons for which the species do not form a unified inventive concept within the art, namely they are etiologically and pathologically distinct disorders with distinct symptoms and non-overlapping patient populations. Therefore, methods of treatment of these disorders have acquired a separate status in the art. For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown by appropriate explanation of separate status in the art as defined in MPEP § 808.02.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

2. Applicant has not provided identification of the claims encompassing the elected invention (37 CFR 1.143). It is believed that claims 17, 18, 22-24 and 26-32 read upon the elected invention. Claims 19-21, 25, 33-48, 54-63 and 96-100 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 5, 2009.

3. Claims 17, 18, 22-24 and 26-32 will be examined upon their merits in the instant office action.

Claim Objections

4. Claims 19-21, 25, 33-48, 54-63 and 96-100 are objected to because of the following informalities: The claims lack a proper Status Identifier as set forth in 37 CFR 1.121(c). The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number by one of the following status identifiers: (original), (currently amended), (previously presented), (canceled), (withdrawn), (new), or (not entered). Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 26-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 26-32 recites GALR2-specific agonist wherein the GALR2-specific agonist has a binding affinity for GALR2 of between 0 and 100 μM and greater than 30-fold binding specificity for GALR2 over GALR1; has a binding affinity for GALR2 of between 0 and 100 μM and greater than 50-fold binding specificity for GALR2 over

GALR1; has a binding affinity for GALR2 of between 0 and 100 μM and greater than 100-fold binding specificity for GALR2 over GALR1; has greater than 30-fold binding specificity for GALR2 over GALR3; has greater than 50-fold binding specificity for GALR2 over GALR3; has greater than 100-fold binding specificity for GALR2 over GALR3; or wherein the GALR2-specific agonist has a binding affinity for GALR2 of between 0 and 1 μM. The claims do not require that the "GALR2-specific agonist" possess any particular conserved structure or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules defined by affinity and the instant specification fails to describe the molecules that are encompassed by the genus of the claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of specific examples of GALR2 agonists: AR-M1896 (also known in the art at the galanin 2-11 peptide), the galanin 1-15 peptide and galanin 1-16 peptide (paragraph [0037]). The claims, however, encompass methods comprising administration of any GALR2-specific agonist that has a binding affinity for GALR2 of between 0 and 100 μM and greater than 30-fold binding specificity for GALR2 over GALR1; has a binding affinity for GALR2 of between 0 and 100 μM and greater than 50-fold binding specificity for GALR2 over GALR1; has a binding affinity for GALR2 of between 0 and 100 μM and greater than 100-fold binding specificity for GALR2 over GALR1; has greater than 30-fold binding specificity for

GALR2 over GALR3; has greater than 50-fold binding specificity for GALR2 over GALR3; has greater than 100-fold binding specificity for GALR2 over GALR3; or wherein the GALR2-specific agonist has a binding affinity for GALR2 of between 0 and 1 μM. Therefore, the claims are not limited to specific molecules with known structure, but rather, the claims merely require the claimed methods employ molecules that have the requisite binding affinity.

In order to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of binding affinity. There is not even identification of any core galanin structure that must be conserved for activity. As stated above, a limited number of molecules are disclosed within the specification, namely AR-M1896, the galanin 1-15 peptide and galanin 1-16 peptide (paragraph [0037]). However, the specification fails to provide a description of these agonists with respect to their binding affinities for the different galanin receptor subtypes. Accordingly, in the absence of sufficient recitation of the distinguishing identifying binding affinity characteristics, the specification does not provide adequate written description of the claimed genus or GALR2-specific agonists.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date

sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of GALR2-specific agonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity (i.e. binding affinity) as part of the invention and a reference to a potential method of isolating or screening, such as referenced in paragraph [0039]. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. Therefore claims 26-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement

7. Claims 17, 18, 22-24 and 26-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating brain injury or damage caused by direct trauma to the spinal cord comprising intrathecal administration of AR-M1896, does not reasonably provide enablement for the method for the treatment of any other brain injury, damage or disease including instantly-elected

Multiple Sclerosis comprising administering any other GALR2-specific agonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be given their broadest reasonable interpretation that is consistent with the specification. See MPEP 2111 [R-5], which states: During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification." Phillips v. AWH Corp., 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005). See also In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more

broadly than is justified. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969).

The nature of the invention is a method for treating brain damage, disease or injury. Claim 17 broadly encompasses methods of treatment of *any* brain injury, damage or disease comprising administering *any* GALR2-specific agonist. The specification states,

> "The invention relates especially, but not exclusively, to protecting or treating the brain from the deleterious effects of(a) embolic, thrombotic or haemorrhagic stroke; (b) direct or indirect trauma to the brain or spinal cord; (c) surgery to the brain or spinal cord; (d) ischaemic or embolic damage to the brain resulting from cardiopulmonary bypass surgery, renal dialysis and reperfusion brain damage following myocardial infarction; (e) diseases of the brain that involve neuronal damage and/or cell death, such as Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, vCJD (variant Creutzfeld Jacob Disease); (f) immunological, chemical or radiation damage to the brain such as that caused by bacterial or viral infections, alcohol, chemotherapy for tumours and radiotherapy for turnouts".

Therefore the breadth of the claims encompasses a vast array of etiologically and pathologically distinct diseases or damage/injuries, including treatment of genetically inherited diseases and congenital damage. Furthermore many of the encompassed diseases/injuries have no nexus to GALR2 activity. Depending claims limit the etiology of the disease, damage or injury, with claim 22 being drawn to the instantly-elected disease of Multiple Sclerosis. Further depending claims limit the agonist to a polypeptide that comprises a portion of the galanin protein, or specifically where the agonist is AR-M1896, and then further define the agonist in terms of its binding affinity for GALR2 over GALR1/GALR3. One of ordinary skill in the art would not be apprised as to how to practice the method for the treatment of any brain disease

or damage comprising administering any GALR2-specific agonist with a reasonable expectation of success.

As opposed to the claims, what is disclosed about the claimed method is narrow: The invention is based on following finding: "galanin acts as an endogenous neuroprotective factor to the hippocampus ... GALR2 is the principal receptor subtype that mediates these protective effects. These data indicate that a GALR2-specific agonist will have therapeutic uses in the treatment or prevention of various forms of brain injury, damage or disease" (Specification, page 25). However, the instant specification is not found to be enabled for the method as claimed, for the following reasons. The instant specification provides neither enough guidance or direction, nor working examples, which would show that the claimed method was successfully achieved for treatment commensurate in scope with the claims. The instant specification provides only one in vivo working example: Galanin over-expressing animals have decreased cell death upon Kainic Acid-induced excitotoxicity as compared to wild type animals (Example 1). All of the other examples utilize organotypic cultures and teach: Galanin knockout organotypic cultures display increased cell death upon staurosporine treatment (Example 2) and increased in galanin overexpressing animals as compared to strain-matched wild-type (Example 3); Galanin co-administered with staurosporine provides neuroprotection in organotypic cultures (Example 4); The GALR2-specific agonist AR-M1896 is neuroprotective when administered with staurosporine in organotypic cultures (Example 5); Galanin is neuroprotective upon fibrillar amyloid-beta-induced toxicity (Example 6); and galanin is neuroprotective in the

EAE animal model for Multiple Sclerosis (Example 7). The sole in vivo working example provided teaches administration of galanin, which is not GALR2-specific but is known in the art to bind all of the galanin receptors. There is no guidance or direction as to how to treat any brain injury, damage or disease comprising in vivo administration of a GALR2-specific agonist. Therefore, from what is disclosed within the specification, one of ordinary skill in the art would not know how to use the method as claimed for the in vivo treatment of *any* brain injury, damage or disease comprising administering *any* GALR2-specific agonist. Absent such guidance within the instant disclosure, a skilled artisan would rely upon what was known in the art at the time of filing regarding GALR2-specfic agonists and treatment of brain injury, damage or disease.

The state of the art at the time of filing recognized that the GALR2-specific agonist of the claims, AR-M1896, was effective to treat neuropathic pain following spinal cord injury (Liu et al. 2001, cited in previous Office action). However, there was nothing of record to suggest a role for GALR2 activation in the etiology or pathology of the vast array of brain diseases, damage or injury encompassed by the claims. Nor is there anything of record to suggest a nexus between galanin receptors and the pathology of the instantly-elected Multiple Sclerosis. Absent specific guidance within wither the instant disclosure or the prior art, one of ordinary would have to make a substantial inventive contribution in order to practice the invention commensurate in scope with the claims.

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation

of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech, Inc, v. Novo Nordisk*, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

In order to successfully use the method for the treatment of any brain injury, damage or disease, a skilled artisan would have to first demonstrate a nexus between galanin receptor (GALR2) activation and disease/damage/injury pathology. The artisan would then have to identify GALR2 specific agonists and demonstrate that administration in vivo, by any means (i.e. subcutaneous or oral), is successful to treat the pathology. Such experimentation goes beyond that which is considered routine within the art, and requires undue experimentation in order to practice the method as claimed. The instant specification is not enabling because one cannot follow the

guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 17, 18, 23, 24, 26, 27, 28 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al. (2001) cited in previous Office action mailed May 5, 2009, as evidenced by Bennett et al., Current Protocols in Neuroscience, Chapter 9: unit 9.14, May 2003.

10. Claims 17, 18, 23 and 24 are drawn to a method for treating brain injury, damage or disease comprising administering an effective amount of a GALR2-specific agonist to an individual in need of such treatment; wherein the brain injury or damage is caused by direct or indirect trauma or surgery to the brain or spinal cord; wherein the GALR2-specific agonist is a polypeptide comprising a portion of the galanin amino acid sequence; and wherein the GALR2-specific agonist is AR-M1896. Claims 26, 27, 28 and 32 are drawn to a GALR2-specific agonist that has a binding affinity for GALR2 between 0 and 100 μM or between 0 and 1 μM and also has a greater than 30-fold, 50-fold or 100-fold specificity for GALR2 over GALR1.

11. The Liu et al. prior art teaches treatment of neuropathic pain following sciatic nerve injury. Specifically, the reference teaches intrathecal administration of the instantly-claimed AR-M1896 (claim 24) for the treatment of neuropathic pain. AR-M1896 is disclosed as comprising residues 2-11 of the C-terminal truncated galanin protein (page 9960, column 2, lines 5-8), thus, teaching the agonist comprising a portion of the galanin amino acid sequence as required by claim 23. The AR-M1896 of the claim is further disclosed as having a binding affinity for GALR2 of 1.76 nM and a 500-fold selectivity for GALR2 over GALR1 (Table 1). Therefore, the agonist of the reference teaches each of the requirements of claims 26, 27, 28 and 32.

12. The Bennett reference is relied upon to demonstrate that the method for inducing sciatic nerve injury as taught by the Liu et al. reference, was well-known in the art to "damage motor neuron axons" from cell bodies within the dorsal root ganglion and it "produces at least 16 different contralateral phenomena in the nerve, dorsal root ganglion, spinal cord dorsal horn and sympathetic ganglion" (page 9.14.12 top of column 2). The afferents from the dorsal root ganglion relay sensory information to the central nervous system. Therefore, the method as taught by Liu et al., fully anticipates the treatment of brain injury, damage or disease encompassed by the instant claims and, in particular, teaches damage or injury caused by "direct or indirect trauma ... to the brain or spinal cord" as required by claim 18.

13. Thus, the instantly claimed method fails to distinguish over that of the prior art and Claims 17, 18, 23, 24, 26, 27, 28 and 32 are rejected as being anticipated by Liu et al. (2001).

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-W and F 5:30 to 2, TELEWORK-Thursdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
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/John D. Ulm/

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